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# Phylogenetic relationships in the family *Streptomycetaceae* using multi-locus sequence analysis

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# Abstract

The family *Streptomycetaceae*, notably species in the genus *Streptomyces*, have long been the subject of investigation due to their well-known ability to produce secondary metabolites. The emergence of drug resistant pathogens and the relative ease of producing genome sequences has renewed the importance of *Streptomyces* as producers of new natural products and resulted in revived efforts in isolating and describing strains from novel environments. A previous large study of the phylogeny in the *Streptomycetaceae* based on 16S rRNA gene sequences provided a useful framework for the relationships among species, but did not always have sufficient resolution to provide definitive identification. Multi-locus sequence analysis of 5 house-keeping genes has been shown to provide improved taxonomic resolution of *Streptomyces* species in a number of previous reports so a comprehensive study was undertaken to evaluate evolutionary relationships among

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species within the family *Streptomycetaceae* where type strains are available in the ARS Culture Collection or genome sequences are available in GenBank. The results of the analysis supported the distinctiveness of *Kitasatospora* and *Streptacidiphilus* as validly named genera since they cluster outside of the phylogenetic radiation of the genus *Streptomyces*. There is also support for the transfer of a number of *Streptomyces* species to the genus *Kitasatospora* as well for reducing at least 31 species clusters to a single taxon. The multi-locus sequence database resulting from the study is a useful tool for identification of new isolates and the phylogenetic analysis presented also provides a road map for planning future genome sequencing efforts in the *Streptomycetaceae*.

#### Keywords

MLSA; Streptomyces; Kitasatospora; Streptacidiphilus; Systematics

#### Introduction

Species within the family *Streptomycetaceae*, notably those in the genus *Streptomyces*, have been the subject of investigations for over a century, particularly following the discovery of their prodigious ability to produce antibiotics. The importance and role of *Streptomyces* in nature and biotechnology have been thoroughly reviewed elsewhere and thus will not be discussed here. However it was noted that 58 new Streptomyces species have been described to date since 2012 and Streptomyces were mentioned more than 22,000 times in the patent literature worldwide during the same period. The emergence of multiple drug resistant pathogens and relative ease of generating draft whole genome sequences from microorganisms has elevated the importance of Streptomyces strains as producers of valuable new natural products and resulted in renewed efforts in isolating and describing strains from new and novel environments. As thoroughly discussed by Labeda et al. (2012) in their study of the 16S rRNA gene phylogeny of the Streptomycetaceae, the systematics and taxonomy of the members of the family have had a long and meandering history, from one based largely on morphological characteristics, through numerical taxonomic analysis of large numbers of physiological (i.e., phenotypic) traits, and finally on to use of molecular genetic methods such as DNA:DNA hybridization and 16S rRNA gene sequencing. The 16S rRNA gene phylogeny provides a useful framework for inferring the relationships between species, but did not always seem to have enough taxonomic resolution to provide definitive identifications in the absence of DNA-DNA relatedness data. The observation that species of the genera *Kitasatospora* and *Streptacidiphilus* were found within the phylogenetic radiation of Streptomyces based on 16S rRNA gene sequences led some to question the validity of these genera (Kämpfer 2012). The use of multi-locus sequence analysis (MLSA) has been clearly demonstrated to provide the necessary resolution, comparable to that of DDH, for species discrimination within the Streptomycetaceae (Guo et al. 2008; Rong et al. 2009, 2010; Rong and Huang 2010, 2012, 2014). MLSA has been used recently to clarify the taxonomic position of members of a number of the 16S rRNA gene phylogeny clades including Clade 126, the Streptomyces albus clade (Labeda et al. 2014), and Clade 6, the Streptomyces hirsutus clade (Labeda et al. 2016), as well as a study of the strains within the NRRL Culture Collection identified as Streptomyces scabiei (Labeda 2016). A comprehensive study was therefore undertaken to evaluate the phylogenetic relationship of

all taxa within the family *Streptomycetaceae* whose type strains were currently available in the ARS (NRRL) Culture Collection, as well as those type strains having draft genome sequences available in the public databanks.

# Methods

The strains sequenced in the study were obtained from the ARS (NRRL) Culture Collection, Peoria, IL, USA where they had been maintained in long-term storage as lyophilized stocks and are listed in Supplemental Table S1. Strains were cultivated on yeast extract-malt extract agar (YM) ISP-2 medium (Shirling and Gottlieb 1966) at 28 °C for generation of biomass for DNA extraction. Some data were obtained from previous MLSA studies of from genome sequences deposited in NCBI for strains sequenced elsewhere.

Genomic DNA was isolated from all strains using UltraClean<sup>®</sup>Microbial DNA isolation kits (MoBio Labs, Carlsbad, CA) following the instructions of the manufacturer. Partial sequences of the house-keeping genes *atpD* (ATP synthase F1, beta subunit), *gyrB* (DNA gyrase B subunit), *rpoB* (RNA polymerase beta subunit), *recA* (recombinase A) and *trpB* (tryptophan synthetase, beta subunit) were amplified and sequenced using the primers and protocols described previously by Labeda et al. (2014). Amplified products were purified using ExoSAP-IT (Affymetrix, Santa Clara, CA), sequenced using BigDye 3.1 on an ABI model 3730 sequencer and assembled using Sequencher version 5.2 (Gene Codes, Ann Arbor, MI). The gene sequences for the 5 house-keeping loci for strains sequenced locally were deposited in Genbank (see Supplemental Table S1).

The draft genome sequences of a number of strains were also determined in the course of the present study. Libraries were prepared with genomic DNA isolated as described above using a Nextera XT DNA library preparation kit (Illumina, San Diego, CA) following the manufacturer's instructions. The library preparations were sequenced with a MiSeq Desktop Sequencer (Illumina, San Diego, CA) and the resulting short sequence reads were trimmed for quality and removal of adapter sequences, and subsequently *de novo* assembled with CLC bio Genomics Workbench version 8.0.1 (CLC bio, Waltham, MA). The draft genome sequences have been deposited in the NCBI Whole Genome Shotgun database (See Supplementary Table S2).

The gene sequences for the 5 house-keeping loci for strains sequenced locally were organised using Bacterial Isolate Genomic Sequence Database (BIGSdb) version 1.12.3 (Jolley and Maiden 2010) on the ARS Microbial Genomic Sequence Database server (https:// 199.133.98.43). Where available (see Supplemental Table S2), genome sequences were up-loaded into the sequence bin for the respective strains in the BIGSdb isolate database. The genome sequences were scanned within BIGSdb for house-keeping loci, the specific sequence regions were tagged and the allele sequences and respective allele designations added to the sequence database if new alleles were found. The strain record was then updated with the matching allele id for each locus in the strain database. The sequences for the alleles of the loci for all strains in the study were individually aligned with MAFFT (Katoh and Standley 2013), subsequently concatenated head to tail in-frame, and exported in FASTA format, providing a dataset of 692 strains and 2608 positions.

Phylogenetic relationships were constructed from the partitioned gene data in IQ-Tree version 1.41 (Nguyen et al. 2015) using the Maximum Likelihood based on the General Time Reversible model (Nei and Kumar 2000), GTR + F + I + G4, which had been determined to be the optimal model for these data during the model test phase of analysis. The trees were subjected to 1000 ultrafast bootstrap replications (Minh et al. 2013) followed by 1000 replications of assessment of branch supports with single branch tests with SH-like approximate likelihood ratio test (Guindon et al. 2010).

MLSA evolutionary distances were determined using MEGA 6.0 (Tamura et al. 2013) by calculating the Kimura 2-parameter distance (Kimura 1980) and are shown in Supplemental Table S3 for each strain pair. Strain pairs having 0.007 MLSA evolutionary distance were considered conspecific based on the guideline empirically determined by Rong and Huang (2012) that this MLSA distance (Kimura 2-parameter distance) computed from the partial sequences of these house-keeping loci equates to 70% DNA–DNA homology.

# **Results and discussion**

The phylogenetic relationship of species within the *Streptomycetaceae* based on the partial sequences of the 5 house-keeping loci can be seen in Fig. 1a–j. The node labels also include the taxon's clade designation from the 16S rRNA gene sequence phylogenetic study of Labeda et al. (2012) as well as the clade assignment in the numerical taxonomic study of Williams et al. (1983), if included in that study. The clades designated on the trees were defined based on an MLSA distance 0.007 (shown in Supplemental Table S3), indicating that these represented the same species. Bootstrap values less than 95% or branches having SH-aLRT less than 85% were not shown on the tree as recommended by the developers of IQ-Tree.

There is generally good correlation between the phylogenetic relationships observed between species in the individual clades (Fig. 1a-j) with those observed in our previous phylogenetic study based on 16S rRNA gene sequences (Labeda et al. 2012). Not surprisingly, there is also fairly good correlation within clades to those assigned in the numerical taxonomic study of Williams et al. (1983), which could have been expected since the MLSA study should correlate well with observed phenotype. A major difference from the phylogenetic tree constructed using 16S rRNA sequence data is that those strains identified as species within the genera Kitasatospora and Streptacidiphilus are clearly observed (Fig. 1a) to fall outside of the radiation of the genus Streptomyces, thus confirming their validity and making the proposal of Kämpfer (2012) that these are genera incertae sedis unlikely. Girard and colleagues previously reported (Girard et al. 2014) evolutionary genetic changes in conserved developmental genes between Kitasatospora and Streptomyces that supported the validity of the genus *Kitasatospora* and their proposal was confirmed not only by the phylogenetic relationships shown in Fig. 1a but by a scan of the genomes held in the ARS Microbial Genomic Sequence database (http://199.133.98.43) in the present study that demonstrated that the *bldB* gene locus was absent in strains identified as *Kitasatospora* or Streptacidiphilus as they suggested. The 5-gene phylogeny shown in Fig. 1a also makes it quite evident that the type strains of many validly named *Streptomyces* species clearly belong within the genus Kitasatospora including: Streptomyces aburaviensis Nishimura

et al. 1957, Streptomyces albolongus Tsukiura et al. 1964, Streptomyces aureofaciens Dugger 1948 (with Streptomyces avellaneus Baldacci and Grein 1966 as a later synonym), Streptomyces chrysomallus subsp. fumigatus Frommer 1959, Streptomyces cinereorectus Terekhova and Preobrazhenskaya 1986, Streptomyces herbaricolor Kawato and Shinobu 1959, Streptomyces misakiensis Nakamura 1961, Streptomyces psammoticus Virgilio and Hengeller 1960, and Streptomyces purpeofuscus Yamaguchi and Saburi 1955. Strain NRRL B-1588<sup>T</sup>, the type strain of *Streptomyces cinnamonensis* subsp. *cinnamonensis*, was also unexpectedly found within the Kitasatospora clade but equivalent type material from another culture collection must be obtained and analysed before any proposal is made to reclassify this strain. It is interesting to note that NRRL B-16,504, a strain deposited into the ARS Culture Collection as a proposed new species 'Kitasatospora papulosa' but demonstrated as a member of the species Streptomyces pratensis in this study (Fig. 1i) was found to contain an allele of the *bldB* locus. *Streptacidiphilus* species form a distinct, well supported clade that contains all of the taxa for which sequences were available. Strain NRRL B-24555, an isolate from cave soil collected on Jeju Island, Korea and deposited by S. D. Lee as the type strain of a possible new species to be named *Streptacidiphilus jeojiense* but never published, appears distinct from the other Streptacidiphilus species sequenced and likely represents a new species in this genus but further characterisation of morphological, chemotaxonomic and physiological traits will be necessary to fully describe it.

It is notable that both strains of *Streptomyces griseoplanus* that were included in the present study, representing the type strain and the International *Streptomyces* Project (ISP) strain, appear to be phylogenetically distinct from the genera *Kitasatospora, Streptacidiphilus* while also lacking the gene *bldB* and outside of the phylogenetic radiation of *Streptomyces* sensu stricto. Although a draft genome sequence has been determined for the type strain (NRRL B-3064<sup>T</sup>), further morphological, chemotaxonomic, and physiological study is necessary to formally propose a new genus for these strains. Likewise it will be interesting for future studies to address the relationships of the type species of the recently described genus *Allostreptomyces* (Huang et al. 2016) to other genera of the family *Streptomycetaceae* using whole genome sequencing and MLSA.

It is interesting to observe that certain morphological traits of *Streptomyces* species correlate with phylogenetic relationships observed from MLSA, including the clustering of those taxa having rugose spore surface ornamentation into a single well supported clade (Fig. 1a), while those exhibiting verticillate sporophore structures, originally described as species within the genus *Streptoverticillium*, are also found within another well-supported clade (Fig. 1c). Both clades are found within the radiation of the genus *Streptomyces*, as currently defined, and any proposal toward subdividing *Streptomyces* will require the availability of far more genome sequences for representative type strains for analysis.

Many of the clades presented in Fig. 1a–j illustrate species synonymies for which proposals have already been published. These include: *Streptomyces albidoflavus* (Rong et al. 2009) with *Streptomyces canescens, Streptomyces champavatii, Streptomyces coelicolor, Streptomyces felleus, Streptomyces globisporus* subsp. *caucasicus, Streptomyces griseus* subsp. *solvifaciens, Streptomyces limosus, Streptomyces odorifer* and *Streptomyces sampsonii* as later heterotypic synonyms, with the addition of *Streptomyces galilaeus* 

CGMCC 4.1320<sup>T</sup>, *Streptomyces sioyaensis* CGMCC 4.1306<sup>T</sup> and *Streptomyces vinaceus* CGMCC 4.1305<sup>T</sup> in the present study (Fig. 1a); *Streptomyces albovinaceus* (Rong and Huang 2010), with Streptomyces griseinus and Streptomyces mediolani as later heterotypic synonyms, now includes *S. globisporus* subsp. *globisporus* NRRL B-2872<sup>T</sup> in the present study (Fig. 1i) which has priority over S. albovinaceus requiring an emended description after genome sequences are obtained for all and DDH determinations are performed; S. albus (Labeda et al. 2012) with Streptomyces almquistii, Streptomyces flocculus, Streptomyces gibsonii and Streptomyces rangoonensis as later heterotypic synonyms (Fig. 1b); Streptomyces anulatus (Rong and Huang 2010) with Streptomyces praecox as a later heterotypic synonym including Streptomyces chrysomallus subsp. chrysomallus NRRL 2250<sup>T</sup> and ATCC 11523<sup>T</sup> in the present study (Fig. 1j), confirming the observation of Lanoot et al. (2005); Streptomyces atroolivaceus (Rong and Huang 2010) with Streptomyces olivaceoviridis as a later heterotypic synonym (Fig. 1i); Streptomyces bacillaris (Rong and Huang 2010) with Streptomyces griseobrunneus as a later heterotypic synonym, as well as Streptomyces cavourensis subsp. cavourensis NRRL ISP-5300<sup>T</sup> in the present study (Fig. 1i); Streptomyces castelarensis (Rong and Huang 2012) with Streptomyces antimycoticus and Streptomyces sporoclivatus as later heterotypic synonyms including Streptomyces mordarskii NRRL B-1346<sup>T</sup> in the present study (Fig. 1a); Streptomyces cyaneofuscatus (Rong and Huang 2010) with Streptomyces cavourensis subsp. washingtonensis as a later heterotypic synonym, but not Streptomyces fluorescens as proposed by Rong and Huang (2010) (Fig. 1j); Streptomyces ehimensis (Rong and Huang 2012) with Streptomyces luteoverticillatus as a later heterotypic synonym (Fig. 1c); Streptomyces fimicarius (Rong and Huang 2010) with Streptomyces acrimycini, Streptomyces baarnensis, Streptomyces *caviscabies* and *Streptomyces flavofuscus* as later heterotypic synonyms, including Streptomyces bohaiensis NRRL B-24956<sup>T</sup> in the present study (Fig. 1j); Streptomyces flavovirens (Rong and Huang 2010) with Streptomyces flavogriseus as a later heterotypic synonym including *Streptomyces nigrifaciens* NRRL B-2094<sup>T</sup> in the present study (Fig. 1i); S. griseus (Rong and Huang 2010) with Streptomyces erumpens, 'Streptomyces ornatus' and Streptomyces setonii as later heterotypic synonyms (Fig. 1j); Streptomyces hirsutus (Labeda et al. 2016) with Streptomyces cyanoalbus as a later heterotypic synonym (Fig. 1f); Streptomyces hygroscopicus (Rong and Huang 2012) with Streptomyces demainii, Streptomyces endus and Streptomyces sporocinereus as later heterotypic synonyms (Fig. 1a); Streptomyces javensis (Rong and Huang 2012) with Streptomyces yogyakartensis as a later heterotypic synonym (Fig. 1a); Streptomyces microflavus (Rong and Huang 2010) with Streptomyces alboviridis, S. griseus subsp. alpha, S. griseus subsp. cretosus and Streptomyces luridiscabiei as later heterotypic synonyms including Streptomyces lipmanii NRRL B-1229<sup>T</sup>, Streptomyces willmorei NRRL B-1332<sup>T</sup> (confirming the proposals of Lanoot et al. (2005) and Labeda et al. (2014)) and Streptomyces thioluteus NRRL B-1667<sup>T</sup> in the present study (Fig. 1j); *Streptomyces nigrescens* (Rong and Huang 2012) with Streptomyces libani subsp. libani as a later heterotypic synonym; Streptomyces prasinopilosus (Labeda et al. 2016) with Streptomyces emeiensis as a later heterotypic synonym (Fig. 1f); Streptomyces prasinus (Labeda et al. 2016) with Streptomyces bambergiensis as a later heterotypic synonym (Fig. 1f); Streptomyces puniceus (Rong and Huang 2010) with Streptomyces californicus and Streptomyces floridae as later heterotypic synonyms (Fig. 1i); Streptomyces rectiverticillatus (Rong and Huang 2012)

with *Streptomyces aureoversilis* as a later heterotypic synonym (Fig. 1c); *Streptomyces rhizosphaericus* (Rong and Huang 2012) with *Streptomyces asiaticus*, *Streptomyces cangkringensis* and *Streptomyces indonesiensis* as later heterotypic synonyms (Fig. 1a).

This phylogenetic study also supported proposals in previous studies for elevating former subspecies to new species, including *Streptomyces glebosus*, formerly *Streptomyces hygroscopicus* subsp. *glebosus* (Rong and Huang 2012) (Fig. 1b), *Streptomyces ossamyceticus*, formerly *S. hygroscopicus* subsp. *ossamyceticus* (Rong and Huang 2012) (Fig. 1h) and *Streptomyces pathocidini*, formerly *S. albus* subsp. *pathocidicus* (Labeda et al. 2014) (Fig. 1b).

In the present study some potentially misidentified collection strains were identified based on phylogenetic position and an MLSA distance 0.007. *Streptomyces narbonensis* NRRL ISP-5016<sup>T</sup> is identified as a strain of *S. albus* (see Fig. 1b) while the original type strain, NRRL B-1680<sup>T</sup> is found nearest to *Streptomyces zaomyceticus* NRRL B-2038<sup>T</sup> (near *S. venezuelae* in Fig. 1c). As mentioned by Labeda et al. (2012), '*S. albus*' J1074, whose genome has been sequenced, is actually a strain of *Streptomyces albidoflavus* and is found in that clade in Fig. 1i. It is also quite evident that *Streptomyces lydicus* NRRL ISP-5461 is actually a strain of *Streptomyces varsoviensis* because all share identical alleles for the 5 house-keeping loci (Fig. 1c) and are phylogenetically very distant from *Streptomyces lydicus* CGMCC 4.1412<sup>T</sup> (Fig. 1b).

It should also be noted that *Streptomyces fulvissimus* DSM 40593<sup>T</sup> (added from a draft genome sequence) is found in the *Streptomyces microflavus* clade (Fig. 1j), quite distant from *Streptomyces fulvissimus* NRRL B-1453<sup>T</sup> (near *Streptomyces alboflavus* in Fig. 1d) that was sequenced locally. It is not clear in this case which strain represents the actual type of *Streptomyces fulvissimus* and comparison with the type strain acquired from one or more other culture collections will be necessary to clarify this situation.

The relationships shown in the maximum likelihood phylogenetic tree in Fig. 1a–j, constructed from the alignment resulting from concatenation of the partial sequences of the 5 house-keeping loci, where the observed MLSA distances between clade members is also 0.007 suggest that a number of validly named *Streptomyces* species should be considered synonymous although further studies, including the preparation of draft genome sequences and determination of genomic relatedness, are needed to confirm any merging of these taxa.

To simplify the discussion of the results illustrated in this very long phylogenetic tree (Fig. 1), observations on each page of the figure will be discussed in order.

In Fig. 1a, aside from the previously discussed species to be reassigned to *Kitasatospora*, it was observed that *Streptomyces samsunensis* NRRL B-24803<sup>T</sup> represents a later heterotypic synonym of *Streptomyces malaysiensis* NRRL B-24313<sup>T</sup> while *Streptomyces cuspidosporus* NRRL B-5620<sup>T</sup> represents a later heterotypic synonym of *Streptomyces sparsogenes* NRRL 2940<sup>T</sup>. The equivalent strains of *'Streptomyces cattleya'* (NRRL 8057 and DSM 46488) that have genome sequences available in the public databanks clearly represent a distinct species but further morphological, chemotaxonomic and phenotypic characterisation is necessary to prepare a formal species description.

In Fig. 1b, the phylogenetic analysis and observed MLSA distance (0.002) confirmed that *Streptomyces aminophilus* NRRL ISP-5186<sup>T</sup> is a later heterotypic synonym of *Streptomyces cacaoi* subsp. *cacaoi* NRRL B-1220<sup>T</sup> as proposed earlier by Lanoot et al. (2002) based on SDS-PAGE of proteins. It can also be seen that *Streptomyces ochraceiscleroticus* CGMCC 4.1096<sup>T</sup> is equivalent to both *S. ochraceiscleroticus* NRRL ISP-559<sup>T</sup> and *Streptomyces violens* NRRL ISP-5597<sup>T</sup> but not *S. violens* CGMCC 4.1786<sup>T</sup> which will require sequencing of additional type strains of *S. violens* from other collections to clarify the taxonomic status of this species.

In Fig. 1c, it was confirmed that *Streptomyces spitsbergensis* NRRL B-24285<sup>T</sup> is a later synonym of *Streptomyces baldaccii* NRRL B-3500<sup>T</sup> as proposed by Hatano et al. (1997) but the present study supports the revival of Streptomyces griseoverticillatus because it does not appear to represent a later synonym of Streptomyces cinnamoneus as Hatano et al. (1997) proposed. *Streptomyces sapporonensis* DSM 41675<sup>T</sup> appears to be a later synonym of *S. griseoverticillatus* DSM 40507<sup>T</sup>. It can be observed that *Streptomyces* alboverticillatus NRRL B-24281<sup>T</sup> has the later synonyms Streptomyces griseocarneus NRRL B-1350<sup>T</sup> and *Streptomyces septatus* NRRL ISP-5577<sup>T</sup>, *Streptomyces abikoensis* CGMCC 4.1662<sup>T</sup> has the later synonym *Streptomyces kashmirensis* NRRL B-3103<sup>T</sup> and Streptomyces mashuensis DSM 40221<sup>T</sup> has the later synonym Streptomyces kishiwadensis NRRL B-12326<sup>T</sup>. Streptomyces cinnamoneus subsp. albosporus NRRL B-5624 appears to represent a distinct species and S. cinnamoneus subsp. lanosus NRRL B-24290 and S. cinnamoneus subsp. sparsus NRRL B-24291 appear to represent a single new species but it is necessary to determine draft genome sequences for all of the Streptomyces cinnamoneus subspecies for genomic DDH comparisons along with morphological and physiological characterisation before these formal descriptions can be prepared.

In Fig. 1d, it was confirmed that *Streptomyces laceyi* CGMCC 4.1832<sup>T</sup> and *Streptomyces spheroides* NRRL 2449<sup>T</sup> represent later synonyms of *Streptomyces niveus* NRRL 2466<sup>T</sup> as proposed by Tamura et al. (2008). It was also confirmed that *Streptomyces fradiae* NRRL B-1195<sup>T</sup> is an earlier synonym of *Streptomyces roseoflavus* NRRL B-2789<sup>T</sup> as proposed by Lanoot et al. (2004). This section of the tree supports that *Streptomyces aureocirculatus* NRRL B-3324<sup>T</sup> (and NRRL ISP-5386<sup>T</sup>) has the later synonym *Streptomyces glomeroaurantiacus* NRRL B-3375<sup>T</sup>, *Streptomyces coerulescens* CGMCC 4.1597<sup>T</sup> has the later synonym *Streptomyces angustmyceticus* CGMCC 4.0207<sup>T</sup> has the later synonym *Streptomyces angustmyceticus* CGMCC 4.0207<sup>T</sup> has the later synonym *Streptomyces noursei* CGMCC 4.0236<sup>T</sup>. The status of strain *Streptomyces noursei* CGMCC 4.0213<sup>T</sup> is unclear because two other type strains of *S. noursei* are found in the tree at the top of Fig. 1c.

In Fig. 1e it was confirmed that *Streptomyces flaviscleroticus* NRRL B-12173<sup>T</sup> is a later synonym of *Streptomyces minutiscleroticus* NRRL B-12202<sup>T</sup> as proposed by Lanoot et al. (2005). The following observations can also be made: *Streptomyces pseudo-griseolus* NRRL B-3288<sup>T</sup> has the later synonyms *Streptomyces gancidicus* NRRL B-1872<sup>T</sup>, *Streptomyces nashvillensis* NRRL B-2606<sup>T</sup> and *Streptomyces rubiginosus* NRRL B-3983<sup>T</sup>; *Streptomyces althioticus* NRRL B-3981<sup>T</sup> has the later synonyms *Streptomyces griseorubens* NRRL B-3982<sup>T</sup>, *Streptomyces matensis* NRRL B-2576<sup>T</sup> and *Streptomyces* 

phaeogriseichromatogenes NRRL 2834<sup>T</sup>; Streptomyces arabicus NRRL B-1733<sup>T</sup> has the later synonyms Streptomyces erythrogriseus NRRL B-3808<sup>T</sup>, Streptomyces griseoincarnatus NRRL B-5313<sup>T</sup> and Streptomyces variabilis NRRL B-3984<sup>T</sup>; Streptomyces pilosus NRRL ISP-5097<sup>T</sup> has the later synonym Streptomyces flavoviridis NRRL ISP-5153<sup>T</sup>; Streptomyces asterosporus NRRL B-24328<sup>T</sup> has the later synonym Streptomyces aureorectus NRRL B-24301<sup>T</sup>; Streptomyces coelescens NRRL B-12348<sup>T</sup> has the later synonyms Streptomyces anthocyanicus NRRL B-24292<sup>T</sup>, Streptomyces humiferus NRRL B-3088<sup>T</sup>, Streptomyces rameus NRRL B-16924<sup>T</sup>, Streptomyces sannanensis NRRL B-24303<sup>T</sup> and Streptomyces violaceorectus NRRL B-12181<sup>T</sup>. It is noted that 'Streptomyces coelicolor' JI 1147 and 'Streptomyces lividans' TK24 are also strains of *S. coelescens*. In addition, Streptomyces ennisocaesilis NRRL B-16365<sup>T</sup>, Streptomyces geysiriensis NRRL B-12102<sup>T</sup> and Streptomyces vinaceusdrappus NRRL ISP-5169<sup>T</sup> represent later synonyms of Streptomyces rochei NRRL B-2410<sup>T</sup> while Streptomyces daghestanicus NRRL B-5418<sup>T</sup> is a later synonym of Streptomyces griseoviridis NRRL ISP-5229<sup>T</sup>.

In Fig. 1f it should be noted that the thermophilic *Streptomyces* species group into a single clade, continued onto Fig. 1g. It was observed that *Streptomyces roseodiastaticius* CGMCC 4.1788<sup>T</sup> has the later synonyms *Streptomyces tricolor* NRRL B-16925<sup>T</sup> (as proposed by Lanoot et al. 2004) and *Streptomyces bangladeshensis* NRRL B-24326<sup>T</sup>. The following observations can also be made: *Streptomyces olivaceoviridis* NRRL B-12280<sup>T</sup> has the later synonym *Streptomyces corchorusii* NRRL B-12289<sup>T</sup> (also DSM 40340<sup>T</sup>); *Streptomyces murinus* NRRL B-2286<sup>T</sup> has the later synonyms *Streptomyces costaricanus* NRRL B-16897<sup>T</sup> and *Streptomyces griseofuscus* NRRL B-5429<sup>T</sup>; *Streptomyces viridosporus* NRRL ISP-5243<sup>T</sup> has the later synonym *Streptomyces griseomycini* NRRL B-12104<sup>T</sup> (also ATCC 14672<sup>T</sup>); *Streptomyces griseomycini* NRRL B-16369<sup>T</sup> and *Streptomyces graminearus* NRRL B-16369<sup>T</sup> and *Streptomyces graminearus* NRRL B-16369<sup>T</sup> has the later synonyms *Streptomyces griseostramineus* NRRL B-16369<sup>T</sup> has the later synonyme *Streptomyces griseostramineus* NRRL B-12375<sup>T</sup> has the later synonyme *Streptomyces thermovulgaris* NRRL B-12375<sup>T</sup> has the later synonyme *Streptomyces thermonitrificans* NRRL B-12534<sup>T</sup>.

In Fig. 1g it can be observed that *Streptomyces phaeopurpureus* NRRL B-2260<sup>T</sup> (and DSM 40125<sup>T</sup>) is confirmed as a later synonym of *Streptomyces griseorubiginosus* CGMCC 4.1766<sup>T</sup> (and DSM 40469<sup>T</sup>) as proposed in Gauze et al. (1983). The following observations can also be made: *Streptomyces inusitatus* NRRL B-16929<sup>T</sup> has the later synonym *Streptomyces longwoodensis* NRRL B-16923<sup>T</sup> (=DSM 41677<sup>T</sup>); *Streptomyces clavifer* CGMCC 4.1064<sup>T</sup>has the later synonyms *Streptomyces canus* NRRL B-3980<sup>T</sup> (=DSM 40017<sup>T</sup>) and *Streptomyces ciscaucasicus* NRRL ISP 5275<sup>T</sup> (=DSM 40275<sup>T</sup>).

In Fig. 1h it was observed that *Streptomyces goshikiensis* NRRL B-5428<sup>T</sup> has the later synonym *Streptomyces sporoverrucosus* NRRL B-16379<sup>T</sup> and *Streptomyces melanogenes* NRRL B-2072<sup>T</sup> has the later synonym *Streptomyces noboritoensis* NRRL B-12152<sup>T</sup>.

Most relationships in Fig. 1i and 1j have already been discussed earlier with the exception of the observation that *Streptomyces griseolus* (both CGMCC 4.1864<sup>T</sup> and NRRL B-2925<sup>T</sup>) is a later synonym of *Streptomyces halstedii* NRRL B-1238<sup>T</sup> and NRRL ISP-5016<sup>T</sup>) based on presence of identical alleles for all 5 house-keeping loci. It should be noted that

*Streptomyces graminofaciens* CGMCC 4.1359<sup>T</sup> (bottom of Fig. 1h) is shown not to be a later synonym of *Streptomyces halstedii* as was suggested by Rong and Huang (2010).

The phylogenetic analyses performed during the course of this study (see Fig. 1a) support the transfer of those *Streptomyces* species found within the radiation of the genus *Kitasatospora* to that genus and emended descriptions for these follow below. Although it would be optimal to also have phenotypic properties to support the proposed taxonomic changes, no useful traits have been discovered in past studies and gene sequencing capabilities have become ubiquitous and within the reach of most investigators so a gene phylogeny-based classification should be completely acceptable. The taxonomic status of *Streptomyces chrysomallus* subsp. *fumigatus* has been problematic since the Lanoot et al. (2005) proposal that *S. chrysomallus* subsp. *chrysomallus* is a later is synonym of *S. anulatus* which is also supported by the present study (see Fig. 1j). *S. chrysomallus* and represents a new species within *Kitasatospora* for which the name *Kitasatospora fumigata* is proposed below.

The results presented in this study demonstrate the value of MLSA using partial sequences of single-copy house-keeping genes to provide resolution of taxonomic issues in the Streptomycetaceae and could result in a 116 species reduction from the over 780 Streptomyces species currently listed on the List of Prokaryote Names With Standing in Nomenclature (www.bacterio.net). This method has been applied to over 400 uncharacterised strains in the NRRL Culture Collection to date and at least 20 potentially new species have been discovered among the microbial strains collected since the 1950s (Labeda, unpublished obervations). Although there could be criticism of the taxonomic resolution and accuracy in utilising only the limited set of 5 house-keeping genes in the present study, our experience has shown that these loci provide an excellent assessment of the phylogenetic relationships between species in the *Streptomycetaceae*. Moreover, the phylogenetic relationships of 170 strains based on maximum likelihood analysis of the sequences of the 5 genes utilised in this study shows good correlation (See Supplemental Figure S1a-d) with that determined utilizing 1487 core genes (1943,267 bp) extracted from the genome sequences of these strains using the Genome Comparator function of BIGSdb, utilising the well-annotated genome sequence (Genbank FN554889) for S. scabiei RL87.22 (=NRRL B-24449) as the reference and with the core gene threshold set at 90%. Although the number of draft or finished genome sequences for strains in the Streptomycetaceae is continually growing, totalling more than 770 at this time, only about 182 of these are from type strains making definitive whole genome or core gene molecular systematics of the entire family Streptomycetaceae not yet within reach. The alleles of the house-keeping genes utilised in this study can be easily discovered within draft or finished genomes and added to the growing sequence database using the genome scanning capability within the BIGSdb software, making it possible to positively and correctly identify incorrectly named genome strains, such as classifying J1074 as a strain of S. albidoflavus rather than S. albus as reported in the genome databases. Furthermore this database can expanded to include all of the relevant single-copy core genes for the family *Streptomycetaceae* once there are genome sequences available for a representative set of type strains. A major value of the phylogenetic relationships illustrated in Fig. 1a-j, aside from providing taxonomic insight

into the genus *Streptomyces*, is in providing a guide map for selection and prioritising critical species within the Streptomycetaceae for future genome sequencing efforts, as well as highlighting those strains requiring genome sequencing because taxonomic proposals of synonyminity need DDH between strains for confirmation, including many of those identified above. The multigene database has been demonstrated as an important tool for identifying phytopathogenic Streptomyces species when 16 of 43 strains of putative S. scabiei strains in the ARS Culture Collection were confirmed to represent non-pathogenic species while 6 strains possibly represent new phytopathogens (Labeda 2016). We have already demonstrated the usefulness of utilising the genomic sequence database, and the associated phylogeny constructed from the data stored in it, to discover new antibiotic producing strains as well as novel secondary metabolites (Price et al. 2016) in the course of discovery of the new tunicamycin analog, quinvosomycin, and its producing strain. The addition of substantially more *Streptomyces* genomes and expansion of the gene set used for phylogenetic analysis, aside from providing for a phylogenomic revision of the systematics of the Streptomycetaceae, should make this database an invaluable tool for mining these genomes for hitherto undiscovered natural products.

The ARS Microbial Genomic Sequence Database database is available at http:// 199.133.98.43/. The new names proposed as a result of this study are described below.

Description of Kitasatospora aburaviensis comb. nov.

*Kitasatospora aburaviensis* (a.bu.ra.vi.en'sis. N.L. fem. adj. *aburaviensis* of or belonging to Aburabi, Shiga Prefecture, Japan, the source of the soil from which the microorganism was isolated).

Basonym *Streptomyces aburaviensis* Nishimura, Kimura, Tawara, Sasaki, Nakajima, Shimaoka, Okamoto, Shimohira and Isono 1957<sup>AL</sup>.

The description is that reported in Kämpfer (2012).

The type strain is AS 4.1469<sup>T</sup>, ATCC 23869<sup>T</sup>, BCRC 11617<sup>T</sup>, CBS 280.60<sup>T</sup>, CBS 608.68<sup>T</sup>, CCRC 11617<sup>T</sup>, CECT 3315<sup>T</sup>, CGMCC 4.1469<sup>T</sup>, DSM 40033<sup>T</sup>, IFO 12830<sup>T</sup>, IMET 43031<sup>T</sup>, IMET 43081<sup>T</sup>, ISP 5033<sup>T</sup>, JCM 4170<sup>T</sup>, JCM 4613<sup>T</sup>, KACC 20033<sup>T</sup>, KCTC 9663<sup>T</sup>, LMG 19305<sup>T</sup>, NBRC 12830<sup>T</sup>, Nishimura S-66<sup>T</sup>, NRRL B-2218<sup>T</sup>, NRRL-ISP 5033<sup>T</sup>, VKM Ac-1868<sup>T</sup>.

Description of Kitasatospora albolonga comb. nov.

*Kitasatospora albolonga* (al.bo.lon'ga. L. adj. *albus* white; L. adj. *longus* long; N.L. fem. adj. *albolonga* white and long).

Basonym *Streptomyces albolongus* Tsukiura, Okanishi, Koshiyama, Ohmori, Miyaki and Kawaguchi 1964<sup>AL</sup>.

The description is that reported in Shirling and Gottlieb (1972).

The type strain is AS  $4.1661^{\text{T}}$ , ATCC  $27414^{\text{T}}$ , Bristol-Banyu  $304R7^{\text{T}}$ , CBS  $766.72^{\text{T}}$ , CGMCC  $4.1661^{\text{T}}$ , DSM  $40570^{\text{T}}$ , IFO  $13465^{\text{T}}$ , ISP  $5570^{\text{T}}$ , JCM  $4716^{\text{T}}$ , KCTC  $9676^{\text{T}}$ , KCTC  $9749^{\text{T}}$ , NBRC  $13465^{\text{T}}$ , NRRL B- $3604^{\text{T}}$ , NRRL ISP- $5570^{\text{T}}$ , RIA  $1426^{\text{T}}$ , VKM Ac- $704^{\text{T}}$ .

Description of Kitasatospora aureofaciens comb. nov.

*Kitasatospora aureofaciens* (au.re.o.fa'ci.ens. L. adj. *aureus* golden; L. part. adj. *faciens* producing; L. part. adj. *aureofaciens* producing golden (referring to pigment produced by the vegetative mycelium of the microorganism).

Basonym *Streptomyces aureofaciens* Duggar 1948, 177<sup>AL</sup>; later synonym *Streptomyces avellaneus* Baldacci and Grien 1966, 195<sup>AL</sup>.

The descriptions is that reported in Kämpfer (2012).

The type strain is ATCC 10762<sup>T</sup>, ATCC 23884<sup>T</sup>, CBS 434.51<sup>T</sup>, CECT 3206<sup>T</sup>, CGMCC 4.0568<sup>T</sup>, CIP 57.11<sup>T</sup>, DSM 40127<sup>T</sup>, IFO 12594<sup>T</sup>, IFO 12843<sup>T</sup>, IMET 43577<sup>T</sup>, ISP 5127<sup>T</sup>, JCM 4008<sup>T</sup>, JCM 4624<sup>T</sup>, KACC 20180<sup>T</sup>, Lederle Labs A-377<sup>T</sup>, LMG 5968<sup>T</sup>, NBRC 12594<sup>T</sup>, NCIB 8234<sup>T</sup>, NRRL ISP-5127<sup>T</sup>, RIA 1129<sup>T</sup>, Waksman 3708<sup>T</sup>.

Description of Kitasatospora cinereorecta comb. nov.

*Kitasatospora cinereorecta* (ci.ne.re.o.rec'ta. L. adj. *cinereus* similar to ashes, ash-colored; L. adj. *rectus* straight; N.L. fem adj. *cinereorecta* ash-colored, straight.)

Basonym *Streptomyces cinereorectus* Terekhova and Preobrazhenskaya 1986, 574<sup>AL</sup>.

The descriptions is that reported in Kämpfer (2012).

The type strain is AS 4.1622<sup>T</sup>, ATCC 43679<sup>T</sup>, CGMCC 4.1622<sup>T</sup>, DSM 41469<sup>T</sup>, IFO 15395<sup>T</sup>, INA 5202<sup>T</sup>, JCM 6916<sup>T</sup>, NBRC 15395<sup>T</sup>, NRRL B-16360<sup>T</sup>. Type strain AS 4.1589<sup>T</sup>, CGMCC 4.1589<sup>T</sup>, DOA 1196<sup>T</sup>, DSM 41424<sup>T</sup>, IFO 15394<sup>T</sup>, JCM 3371<sup>T</sup>, KCTC 9705<sup>T</sup>, NBRC 15394<sup>T</sup>, NRRL B-2289<sup>T</sup>.

Description of Kitasatospora herbaricolor comb. nov.

*Kitasatospora herbaricolor* (her.ba.ri'co.lor. L. n. *herbarius* one skilled in plants, a botanist: L. n. *color* color; N. L. adj. *herbaricolor* grass colored green referring to the grass green diffusible pigment produced by the microorganism on chemically defined media).

Basonym Streptomyces herbaricolor Kawato and Shinobu 1959, 114<sup>AL</sup>.

The descriptions is that reported in Kämpfer (2012).

Type strain AS 4.1849<sup>T</sup>, AS 4.1887<sup>T</sup>, ATCC 23922<sup>T</sup>, CBS 424.61<sup>T</sup>, CBS 906.68<sup>T</sup>, CGMCC 4.1849<sup>T</sup>, CGMCC 4.1887<sup>T</sup>, DSM 40123<sup>T</sup>, IFO 12876<sup>T</sup>, IFO 3838<sup>T</sup>, IFO 3932<sup>T</sup>, ISP 5123<sup>T</sup>, JCM 4138<sup>T</sup>, JCM 4645<sup>T</sup>, NBRC 12876<sup>T</sup>, NBRC 3838<sup>T</sup>, NBRC 3932<sup>T</sup>, NCIMB 9837<sup>T</sup>, NRRL B-3299<sup>T</sup>, NRRL ISP-5123<sup>T</sup>, RIA 1126<sup>T</sup>, RIA 654<sup>T</sup>, Shinobu 608<sup>T</sup>, VKM Ac-793<sup>T</sup>.

Description of Kitasatospora misakiensis comb. nov.

*Kitasatospora misakiensis* (mi.sa.ki.en'sis. N.L. fem. adj. *misakiensis* belonging to misaki (referring to Misakicho, Kanagawa Prefecture, Japan, the source of the soil from which the microorganism was isolated).

Basonym Streptomyces misakiensis Nakamura 1961, 86AL.

Description is that reported in Kämpfer (2012).

Type strain AS 4.1437<sup>T</sup>, ATCC 23938<sup>T</sup>, CBS 278.65<sup>T</sup>, CBS 922.68<sup>T</sup>, CGMCC 4.1437<sup>T</sup>, DSM 40222<sup>T</sup>, IFO 12891<sup>T</sup>, ISP 5222<sup>T</sup>, JCM 4062<sup>T</sup>, JCM 4653<sup>T</sup>, KCTC 19951<sup>T</sup>, LMG 19369<sup>T</sup>, NBRC 12891<sup>T</sup>, NCIB 9852<sup>T</sup>, NRRL B-2923<sup>T</sup>, NRRL ISP-5222<sup>T</sup>, RIA 1166<sup>T</sup>, VKM Ac-625<sup>T</sup>.

Description of Kitasatospora psammotica comb. nov.

*Kitasatospora psammotica* (psam.mo'ti.ca. Gr. n. *psammos* sand; N.L. fem. adj. *psammotica* sandy).

Basonym Streptomyces psammoticus Virgilio and Hengeller 1960, 167<sup>AL</sup>.

Description is that reported in Kämpfer (2012).

Type strain is AS 4.1465<sup>T</sup>, ATCC 14125<sup>T</sup>, ATCC 25488<sup>T</sup>, CBS 175.61<sup>T</sup>, CBS 299.65<sup>T</sup>, CBS 916.69<sup>T</sup>, CGMCC 4.1465<sup>T</sup>, DSM 40341<sup>T</sup>, IFO 13076<sup>T</sup>, ISP 5341<sup>T</sup>, JCM 4434<sup>T</sup>, KCTC 19966<sup>T</sup>, Lepetit Labs C17190<sup>T</sup>, NRRL B-3291<sup>T</sup>, NRRL ISP-5341<sup>T</sup>, RIA 1268<sup>T</sup>, RIA 832<sup>T</sup>, VKM Ac-996<sup>T</sup>.

Description of Kitasatospora purpeofusca comb. nov.

*Kitasatospora purpeofusca* (pur.pe.o.fus'ca. L. adj. *purpureus* purple; L. adj. *fuscus* dark, tawny; N.L. fem. adj. *purpeofusca* dark purple referring to the color of the vegetative mycelium).

Basonym Streptomyces purpeofuscus Yamaguchi and Saburi 1955, 207AL.

Description is that reported in Kämpfer (2012).

Type strain is ATCC 23952<sup>T</sup>, CBS 935.68<sup>T</sup>, CGMCC 4.1767<sup>T</sup>, CGMCC 4.1999<sup>T</sup>, DSM 40283<sup>T</sup>, IFO 12905<sup>T</sup>, ISP 5283<sup>T</sup>, JCM 4156<sup>T</sup>, JCM 4665<sup>T</sup>, KCTC 19967<sup>T</sup>, LMG 20283<sup>T</sup>, NBRC 12905<sup>T</sup>, NCIMB 9822<sup>T</sup>, NRRL B-1817<sup>T</sup>, NRRL ISP-5283<sup>T</sup>, RIA 1197<sup>T</sup>, VKM Ac-1825<sup>T</sup>, Yamaguchi H-5080<sup>T</sup>.

Description of Kitasatospora fumigata comb. nov.

Kitasatospora fumigata (fu.ma.ga'ta. L. fem. part. adj. fumigata smoked).

Basonym Streptomyces chrysomallus subsp. fumigatus Frommer 1959, 202AL.

Description is that reported in Kämpfer (2012).

Type strain AS 4.1589<sup>T</sup>, CGMCC 4.1589<sup>T</sup>, DOA 1196<sup>T</sup>, DSM 41424<sup>T</sup>, IFO 15394<sup>T</sup>, JCM 3371<sup>T</sup>, KCTC 9705<sup>T</sup>, NBRC 15394<sup>T</sup>, NRRL B-2289<sup>T</sup>.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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# Abbreviation

DDH

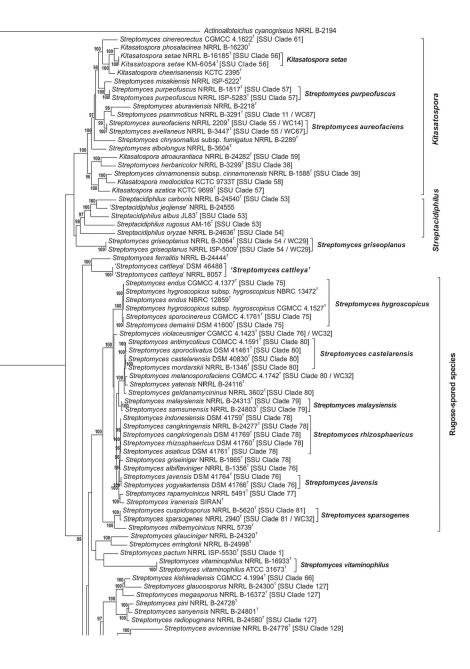
DNA-DNA hybridization

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	1 11 1001				
	Streptomyces specialis GW41-1564 <sup>T</sup> [SSU Clade 129]				
	Streptomyces carpaticus NRRL B-16359 <sup>T</sup> [SSU Clade 128]				
	100 Streptomyces xiamenensis MCCC 1A01550 <sup>T</sup> [SSU Clade 128]				
	Streptomyces aculeolatus NRRL B-24312 <sup>T</sup> [SSU Clade 123]				
	Streptomyces albiaxialis NRRL B-24327 <sup>T</sup>				
	Streptomyces albus NRRL B-1811 <sup>T</sup> [SSU Clade 126 / WC16]				
	Streptomyces gibsonii NRRL B-1335, [SSU Clade 126 / WC16]				
	Streptomyces rangoonensis NRRL B-12378 <sup>T</sup> [SSU Clade 126]				
	Streptomyces almquistii NRRL B-1685 <sup>T</sup> [SSU Clade 126 / WC16]				
	Streptomyces albus NBRC 13014 <sup>T</sup> [SSU Clade 126 / WC16]				
	100 tool Streptomyces albus NRRL B-2208 <sup>1</sup> [SSU Clade 126 / WC16]				
	Streptomyces narbonensis NRRL ISP-5016 <sup>1</sup> [SSU Clade 40 / WC5]				
	Streptomyces flocculus NRRL B-2465 <sup>T</sup> [SSU Clade 126 / WC16]				
	Stratemuse emissible NDDI ISD 5196 <sup>T</sup>				
	Streptomyces cacaoi subsp. cacaoi NRRL B-1220 <sup>1</sup>				
	<sup>33</sup> Streptomyces karpasiensis NRRL B-24899				
	Streptomyces sulphureus NRRL B-1627				
	100 Streptomyces sulphureus DSIN 40104				
	Streptomyces pathocidini NRRL_B-24287' [SSU Clade 120]				
	Streptomyces xinghaiensis S187 <sup>1</sup>				
Ч	Streptomyces guanduensis NRRL B-24617 <sup>1</sup>				
	100 <u>97</u> Streptomyces yanglinensis NRRL B-24620 <sup>7</sup> [SSU Clade 121]				
	SUClade 122]				
	<sup>97</sup> Streptomyces cocklensis NRRL B-24911				
	100 Streptomyces rubidus NRRL B-24619 <sup>†</sup> [SSU Clade 122]				
	Streptomyces ochraceiscleroticus CGMCC 4.1096 <sup>1</sup> [SSU Clade 74]				
	Gueptomyces volens NKRL ISF-5597 Streptomyces ochracelsclefoticus				
	Streptomyces ochraceiscleroticus NRRL ISP-5594 <sup>T</sup> [SSU Clade 74]				
	- Streptomyces violens CONICC 4.1780				
	L Streptomyces purpurogeneiscleroticus CGMCC 4.1929 <sup>°</sup> [SSU Clade 74 / WC40]				
	<sup>™</sup> Streptomyces niger NRRL B-3857 <sup>™</sup> [SSU Clade 73 / WC40]				
	Line Streptomyces sclerotialus NRRL ISP-5269 <sup>7</sup>				
	Streptomyces poonensis NRRL B-2951 <sup>T</sup> [SSU Clade 91 / WC22]				
	Streptomyces politikis riticus CGMCC 4.1438 <sup>™</sup> [SSU Clade 72 / WC42]				
	<sup>99</sup> Streptomyces albofaciens CGMCC 4.1655 <sup>1</sup> [SSU Clade 71 / WC42]				
	Steptomyces chrestonyceticus CGMCC 4.1657 [SSU Clade 71 / WC42]				
	98 <sub>100</sub> Streptomyces chrestomyceticus CGMCC 4.1657 <sup>1</sup> [SSU Clade 71 / WC42] 100 [└_ Streptomyces chrestomyceticus NRRL B-3293 <sup>1</sup> [SSU Clade 71 / WC42]				
	19600 Streptomyces monomycini DSM 41801 [SSU Clade 73] 100 Streptomyces monomycini NRRL B-24309 <sup>7</sup> [SSU Clade 73] Streptomyces enonomycini NRPL WC 2969 <sup>7</sup> [SSU Clade 73]				
	SU Clade 28]				
	u Streptomyces rimosus subsp. rimosus NRRL B-2659 <sup>7</sup> [SSU Clade 72 / WC42]				
	Streptomyces rimosus subsp. rimosus ATCC 10970' [SSU Clade 72 / Wc42] Streptomyces rimosus				
	Streptomyces rimosus subsp. rimosus NRRL ISP-5260 <sup>*</sup> [SSU Clade 72 / WC42]				
	└─ Streptomyces rimosus subsp. paromomycinus CGMCC 4.1760 <sup>1</sup> [SSU Clade 71]				
l	Streptomyces ramulosus CGMCC 4.1434				
	Streptomyces catenulae CGMCC 4.1701				
	100 Streptomyces catenulae NRRL B-2342'				
	100 Streptomyces nigrescens CGMCC 4.1410 <sup>T</sup> [SSU Clade 70 / WC29] Streptomyces nigrescens				
	c Streptomyces libani subsp. libani DSW 40555 [SSO Clade 707 WC29]				
	100 Streptomyces caniferus CGMCC 4.1588 <sup>1</sup> [SSU Clade 21] Streptomyces caniferus NRRL B-1638 <sup>5</sup> [SSU Clade 21] Streptomyces caniferus CGMCC 4.4155 [SSU Clade 21]				
	Streptomyces camierus NRRC 4 1015 [SSU Clade 21]				
	Streptomyces decoyicus CGMCC 4.1915 <sup>7</sup> [SSU Clade 23]				
	tion Streptomyces decoyicus NRRL 2666 <sup>°</sup> [SSU Clade 23]				
	Streptomyces tubercidicus CGMCC 4.1414 <sup>T</sup> [SSU Clade 70 / WC47]				
	Streptomycos debosus CCMCC 4 1873 <sup>T</sup> [SSII Clade 69]				
	Streptomyces platensis CGMCC 4.1975 <sup>T</sup> ISSU Clade 69 / WC291 ]				
	Streptomyces platensis NRRL B-5486 <sup>7</sup> [SSU Clade 69 / WC29] Streptomyces platensis				
	Streptomyces libani subsp. rufus CGMCC 4.1993 <sup>T</sup> [SSU Clade 69]				
	$  $ Streptomyces auratus NRRL 8097 <sup>T</sup>				
	□ Streptomyces lydicus CGMCC 4.1412 <sup>™</sup> [SSU Clade 68]				
	Streptomyces chattanoogensis CGMCC 4.1415 <sup>T</sup> [SSU Clade 68 / WC35]				
	100 Streptomyces chattanoogensis NRRL ISP-5002 <sup>T</sup> [SSU Clade 68 / WC35] Streptomyces chattanoogensis				
	Streptomyces celluloflavus NRRL B-2493 <sup>T</sup> [SSU Clade 31]				
	100 Streptomyces kasugaensis NRRL B-24288				
	Streptomyces albospinus CGMCC 4.1628				
	Streptomyces albulus CGMCC 4.1585 <sup>†</sup> [SSU Clade 67 / WC29]				
	<sup>100</sup> Streptomyces albulus NRRL ISP-5492 <sup>1</sup> [SSU Clade 67 / WC29] Streptomyces albulus				
	Streptomyces albulus NRRL B-5386 [SSU Clade 67 / WC29]				
	Streptomyces yunnanensis NRRL B-24306' [SSU Clade 67]				

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Streptomyces noursei NRRL ISP-5126 <sup>T</sup> [SSU Clade 67]			
Interptomyces nourser ATCC 11455 <sup>T</sup> [SSU Clade 67]     Streptomyces nourser	ei		
Streptomyces diastatochromogenes NRRL B-1698 <sup>T</sup> [SSU Clade 25 / WC19]	7		
Streptomyces aureoversilis CGMCC 4.1641 <sup>T</sup> [SSU Clade 82]			
100 Streptomyces aureoversilis NRRL B-3325 <sup>T</sup> [SSU Clade 82] Streptor	nyces rectiverticillatus		
<sup>100</sup> Streptomyces rectiverticillatus CGMCC 4.1783 <sup>T</sup> [SSU Clade 82 / WC57]			
L Streptomyces hiroshimensis NRRL B-1823°			
100 Streptomyces baldaccii NRRL B-3500 <sup>°</sup> [SSU Clade 50 / WSMC] 100 Streptomyces baldaccii NRRL B-3500 <sup>°</sup> [SSU Clade 50 / WSMC] 110 Streptomyces spitsbergensis NRRL B-24285 <sup>°</sup> [SSU Clade 50]	baldaccii		
Streptomyces biverticillatus NRRL ISP-5272 <sup>T</sup>			
Streptomyces fervens subsp. fervens NRRL ISP-5086			
100100 - Streptomyces roseoverticillatus NRRL B-1993 <sup>T</sup> [SSU Clade 65]			
Streptomyces fervens subsp. melrosporus NRRL 3117			
100 Streptomyces lactis NRRL B-24800 <sup>T</sup>			
Streptomyces lavenduligriseus NRRL B-3173 [SSU Clade 115 / WC34]			
100– Streptomyces morookaensis NRRL B-12429			
Streptomyces lilacinus NRRL B-1968'     100] Streptomyces abikoensis CGMCC 4.1662 <sup>T</sup> Streptomyces abikoensis			
100 Streptomyces kashmirensis NRRL B-3103 J			
Image: Streptomyces ehimensis CGMCC 4.1668 <sup>3</sup> [SSU Clade 63 / WC55]           Image: Streptomyces ulteoverticillatus CGMCC 4.1974 <sup>4</sup> [SSU Clade 63 / WC58]           Image: Streptomyces parvisporogenes NRRL B-5464 <sup>4</sup>	myces ehimensis		
96 Streptomyces parvisporogenes NRRL B-5464			
1001 Streptomyces mashuensis DSM 40221' [SSU Clade 66 / WC55] Streptomyces	machuancis		
···· Caracterio Streptomyces luteosporeus NKRL 2401			
100 Streptomyces ladakanum NRRL ISP-5587 <sup>T</sup>			
Streptomyces mobaraensis NRRL B-3729 <sup>1</sup> Streptomyces luteireticuli NRRL B-12435 <sup>T</sup> [SSU Clade 64 / WC44]			
Streptomyces orinoci NRRL B-3379 <sup>T</sup>			
100 Streptomyces griseoverticillatus DSM 40507 <sup>T</sup> [SSU Clade 62 / WC58] Streptomy			
Streptomyces sapporonensis DSM 41675 <sup>T</sup> [SSU Clade 62]	yces griseoverticiliatus		
100 Streptomyces albireticuli NRRL B-1670 <sup>T</sup> [SSU Clade 51 / WSMC]			
Streptomyces eurocidicus NRRL B-1676 <sup>T</sup> [SSU Clade 51 / WC56]			
Streptomyces stramineus NRRL 12292			
Streptomyces distallicus NRRL 2886 <sup>T</sup> [SSU Clade 52 / WC56]			
C Streptomyces syringae NRRL B-24286' [SSU Clade 52]     []			
Streptomyces kentuckensis NRRL B-1831 [SSU Clade 52]     Streptomyces netropsis NRRL ISP-5259 [SSU Clade 52]     Streptomyces varsoviensis NRRL ISP-5346 [SSU Clade 62]			
100 100 Streptomyces varsoviensis NRRL ISP-5346 <sup>T</sup> [SSU Clade 62]			
Streptomyces lydicus NRRL ISP-5461 <sup>T</sup> [SSU Clade 68 / WC29]	Streptomyces varsoviensis		
Streptomyces varsoviensis NRRL B-3589 <sup>T</sup> [SSU Clade 62]			
Streptomyces ardus NRRL 2817 <sup>T</sup> [SSU Clade 83]			
98 100 Streptomyces blastmyceticus NRRL B-5480' [SSU Clade 83 / WC58]			
Streptomyces cinnamoneus subsp. cinnamoneus NRRL B-1285 <sup>T</sup> [SSU Clade 84 / WC55]			
Streptomyces hachijoensis NRRL B-3106'			
H. Streptomyces cinnamoneus subsp. Janosus NRRI B-24290 <sup>T</sup>			
Streptomyces cinnamoneus subsp. sparsus NRRL B-24290			
$\left  \right  \left  \right _{\Gamma}$ Streptomyces griseocarneus NRRL B-1350 <sup>†</sup>			
g   im Streptomyces alboverticillatus NRRL B-24281 <sup>™</sup> Streptomyces alboverticillatus			
Streptomyces septatus NRRL ISP-5577 <sup>1</sup> J □ Streptomyces olivoverticillatus NRRL B-1994 <sup>T</sup> [SSU Clade 49 / WC2]			
100 <sup>L</sup> Streptomyces viridiflavus NRRL B-1548 <sup>T</sup> [SSU Clade 49]			
Streptomyces olivoreticuli NRRL B-2091 <sup>T</sup>			
95 Streptomyces baliensis NRRL B-24754			
95 Streptomyces fildesensis NRRL B-24828			
Streptomyces exfoliatus CGMCC 4.1407 <sup>T</sup> [SSU Clade 40 / WC5]			
100 Streptomyces gardneri NRRL B-5615 <sup>1</sup> [SSU Clade 40 / WC5] [[ Streptomyces venezuelae NRRL ISP-5230 <sup>↑</sup> [SSU Clade 40 / WC6]			
Streptomyces wedmorensis NRRL 3426 <sup>T</sup> [SSI ] Clade 40]			
<sup>100</sup> Streptomyces narbonensis NRRL B-1680 <sup>T</sup> [SSU Clade 40 / WC5]			
99 Streptomyces zaomyceticus NRRL B-2038 [SSU Clade 40 / WC5]			
Streptomyces aureus NRRL B-2808 <sup>7</sup> [SSU Clade 26 / WC1B]			
Streptomyces venezuelae CGMCC 4.1526 <sup>†</sup> [SSU Clade 40 / WC6] Streptomyces venezuelae CGMCC 4.1526 <sup>†</sup> [SSU Clade 40 / WC6]	ptomyces venezuelae		
Streptomyces venezuelae ATCC 10/12 [SSO Clade 407 WC6]			
Streptomyces bikiniensis NRRL ISP-5581 <sup>1</sup> [SSU Clade 46 / WC64]			
95 Tool Streptomyces bikiniensis NRRL B-2690 <sup>1</sup> [SSU Clade 46 / WC64] Streptomyces vietnamensis GIM4.0001 <sup>1</sup> [SSU Clade 46]			
- Streptomyces tanashiensis CGMCC 4.1924 <sup>T</sup> [SSU Clade 42]			
<sup>95</sup> Streptomyces litmocidini NRRL B-3635 <sup>T</sup> [SSU Clade 40 / WC5]			
Streptomyces filamentosus NRRL B-2114 <sup>T</sup>			
99 100 Streptomyces omiyaensis NRRL B-1587 <sup>T</sup> [SSU Clade 40 / WC5]			
- Streptomyces roseofulvus NRRL B-2729' [SSU Clade 43 / WC14]			
1100 Streptomyces roseolus NRRL B-5424 <sup>T</sup> [SSU Clade 43 / WC5]			

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Streptomyces showdoensis NRRL B-12430 <sup>T</sup> [SSU Clade 45 / WC6]				
100 Streptomyces laurentii NRRL B-24298 <sup>T</sup> [SSU Clade 44]				
99 Streptomyces roseovinais NRRL B-2730				
L Streptomyces viridobrunneus NRRL B-24332 <sup>1</sup> Streptomyces violaceorectus NRRL B-12181 <sup>⊤</sup> [SSU Clade 46 / WC5]				
100 Streptomyces gobitricini NRRL B-12181 [SSU Clade 48]				
97 100 Steptomyces Journal Marce 52555 [SSU Clade 46]				
Streptomyces lavendulocolor NRRL B-3367 <sup>†</sup> [SSU Clade 48 / WC61]				
100 100 Streptomyces luridus NRRL B-5409 <sup>T</sup> [SSU Clade 48 / WC62]				
Streptomyces purpureus NKRL B-5737 [SSU Clade40/ WC65]				
U Streptomyces coeruleoprunus NRRL B-16364 <sup>1</sup> [SSU Clade 85]				
Strentomyces fradiae NRPL B-1195 <sup>T</sup> ISSU Clade 85 / WC681 ]				
<ul> <li>Streptomyces roseoflavus NRRL B-2789<sup>1</sup> [SSU Clade 85]</li> <li>Streptomyces somaliensis NRRL B-12077<sup>1</sup> [SSU Clade 85 / WC70]</li> </ul>				
1000 Streptomyces somaliensis NRRL B-24575' 1000 Streptomyces somaliensis DSM 40738 <sup>7</sup> [SSU Clade 85 / WC70] <b>Streptomyces somaliensis</b>				
Streptomyces toxytricini NRRL B-5426 <sup>7</sup> [SSU Clade 38 / WC61]				
T Streptomyces lacevi CGMCC 4.1832 <sup>™</sup> ISSU Clade 271				
Streptomyces spheroides NRRL 2449 <sup>†</sup> [SSU Clade 27 / WC1B] Streptomyces niveus				
Streptomyces niveus NRRL 2466 <sup>T</sup> [SSU Clade 27 / WC1B]				
100 Streptomyces hebeiensis NRRL B-24445' [SSU Clade 120]				
100 Streptomyces odoppelliji NRPL B-24891				
Streptomyces scopuliridis NRRL B-24574 <sup>T</sup>				
100 Streptomyces albidochromogenes NRRL B-24308 <sup>†</sup> [SSU Clade 41]				
Streptomyces helvaticus NRRL B-12365 <sup>1</sup> [SSU Clade 41 / WC62]     Streptomyces flavidovirens NRRL B-2708 <sup>1</sup> [SSU Clade 41]     Streptomyces flavidovirens				
100 Streptomyces flavidovirens DSM 40150 <sup>T</sup> [SSU Clade 41] Streptomyces flavidovirens				
Streptomyces aureus CGMCC 4.1833 <sup>T</sup> [SSU Clade 26 / WC1B]				
Streptomyces spiroverticillatus CGMCC 4.1749 <sup>†</sup> [SSU Clade 32 / WC6]				
100 Streptomyces cremeus NRRL 3241 <sup>1</sup> [SSU Clade 32 / WC1B]				
100       Loss Streptomyces candidus NRRL ISP-5141'         Streptomyces hypolithicus NRRL B-24669 <sup>T</sup> [SSU Clade 41]				
1001 Streptomyces kanamyceticus CGMCC 4.1441 T				
96 Streptomyces kanamyceticus NRRL B-2535'				
Streptomyces rectiviolaceus NRRL B-16374'				
96 Streptomyces silaceus NRRL B-24166'				
Streptomyces alboniger NRRL B-1832 <sup>T</sup> [SSU Clade 14 / WC1B]				
Streptomyces fulvissimus NRRL B-1453 <sup>T</sup> [SSU Clade 95 / WSMC]				
1001 Streptomyces alboflavus NRRL B-2373 <sup>+</sup> [SSU Clade 95 / WC54]				
Streptomyces flavofungini NRRL B-12307 <sup>1</sup> [SSU Clade 95 / WC42]				
Streptomyces aubosporeus subsp. rabitomycercus NNNC 5-24250				
[10] Streptomyces glomeroaurantiacus NRRL B-3375 <sup>r</sup> [SSU Clade 15 / WC19] Streptomyces aureocirculatus				
SUClade 15 / WC3				
97 Streptomyces aureoverticillatus NRRL B-3326'				
Streptomyces variegatus NRRL B-16380'				
Streptomyces bobili CGMCC 4 1624 <sup>T</sup> [SSU Clade 13]				
[ ] ]				
100 - Streptomyces phaeoluteigriseus NRRL ISP-5182				
Streptomyces novaecaesareae NRRL B-3011 <sup>1</sup> Streptomyces mirabilis NRRL ISP-5553 <sup>7</sup> [SSU Clade 20 / WC45]				
97				
1 Streptomyces olivochromogenes NRRL B-1341 [SSU Clade 20 / WC19]				
[        100 Streptomyces olivochromogenes DSM 40451 [SSU Clade 20 / WC19] ]				
Streptomyces kaempferi NRRL B-59130'				
100 Streptomyces avermitilis DSM 46492 <sup>T</sup>				
Streptomyces prunicolor NRRL B-12281 <sup>*</sup>				
100 Streptomyces prunicolor NBRC 13075				
Streptomyces cyaneus CGMCC 4.1671 <sup>1</sup> Streptomyces coerulescene CGMCC 4.1597 <sup>1</sup> ISSU Clade 114 / WC181 3				
Streptomyces coerulescens CGMCC 4.1597 <sup>†</sup> [SSU Clade 114 / WC18] <sup>100</sup> Streptomyces coerulescuscus NRL B-5417 <sup>†</sup> [SSU Clade 114 / WC18] <sup>100</sup> Streptomyces coerulescuscus NRL B-5417 <sup>†</sup> [SSU Clade 114 / WC18]				
Streptomyces chartreusis NRRL ISP-5085				
□ □ □ □ Streptomyces longisporus NRRL B-5336 <sup>™</sup>				
Streptomyces angustmyceticus CGMCC 4.0207 <sup>1</sup> Streptomyces pluricolorescens CGMCC 4.0236 <sup>1</sup> Streptomyces angustmyceticus				
Streptomyces noursei CGMCC 4.0213 <sup>7</sup> [SSU Clade 67]				

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Streptomyces gancidicus NRRL B-1872<sup>1</sup> [SSU Clade 86] Streptomyces rubiginosus NRRL B-3983<sup>1</sup> [SSU Clade 86 / WC12] Streptomyces nashvillensis NRRL B-2606<sup>5</sup> [SSU Clade 42 / WC5] Streptomyces lusianus NRRL B-2637<sup>1</sup> [SSU Clade 83 / WC12] Streptomyces lusianus NRRL B-5637<sup>1</sup> [SSU Clade 109 / WC44] — Streptomyces althodiastaticus NRRL B-5622<sup>1</sup> [SSU Clade 110 / WC21] — Streptomyces althodias NRRL B-3981<sup>1</sup> [SSU Clade 99 / WC12] Streptomyces althodias NRRL B-3981<sup>1</sup> [SSU Clade 99 / WC12] — Streptomyces materias NRRL B-2576<sup>1</sup> [SSU Clade 100 / WC12] — Streptomyces materias NRRL B-3981<sup>1</sup> [SSU Clade 100 / WC12] — Streptomyces materias NRRL B-3981<sup>1</sup> [SSU Clade 100 / WC12] — Streptomyces materias NRRL B-3981<sup>2</sup> [SSU Clade 100 / WC12] Streptomyces pseudogriseolus Streptomyces althioticus Streptomyces griseorubens NRRL B-3982<sup>°</sup> [SSU Clade 100] Streptomyces phaeogriseichromatogenes NRRL 2834<sup>°</sup> [SSU Clade 101] Streptomyces arabicus NRRL B-1733<sup>°</sup> [SSU Clade 100 / WC12] 100, Streptomyces erythrogriseus NRRL B-3808<sup>T</sup> [SSU Clade 100] [Streptomyces griseoincarnatus NRRL B-5313<sup>T</sup> [SSU Clade 100 / WC13] Streptomyces arabicus Streptomyces griseoincarnatus rurkt. Leval to jour stati Streptomyces variabilis NRRL B-3984<sup>4</sup> [SSU Clade 100] Steptomyces werraensis NRRL B-5317<sup>1</sup> Streptomyces cellulosae NRRL B-2889<sup>1</sup> <sup>100</sup> Streptomyces thermocarboxydus NRRL B-24316<sup>T</sup> [SSU Clade 109] 

 Image: Streptomyces flavoviridis NRRL IS-24316 [SSU Clade 109]

 Jstreptomyces flavoviridis NRRL IS-5037 [SSU Clade 111 / WC28]

 Streptomyces advorviridis NRRL IS-5097 [SSU Clade 111 / WC37]

 Streptomyces malachiolacus NRRL B-16357

 Streptomyces malachiolacus NRRL B-12273

 Streptomyces malachiolacus NRRL B-12273

 Streptomyces malachiolacus NRRL B-242401

 լլ Streptomyces speibonae NRRL B-24240'
 Streptomyces albaduncus NRRL B-24240'
 Streptomyces albaduncus NRRL B-24328' [SSU Clade 110]
 Streptomyces aureorectus NRRL B-24328' [SSU Clade 118]
 Streptomyces calvus NRRL B-24329' [SSU Clade 118]
 Streptomyces calvus NRRL B-2399' [SSU Clade 118 / WC12]
 Streptomyces anthocyanicus NRRL B-24329' [SSU Clade 103]
 Streptomyces anthocyanicus NRRL B-24329' [SSU Clade 103] 100 Streptomyces coelescens NRRL B-12348<sup>T</sup> [SSU Clade 103] Streptomyces violaceorectus NRRL B-12181<sup>T</sup> [SSU Clade 46 / WC5 Streptomyces coelicolor JI 1147 Streptomyces coelescens Streptomyces bunifers NRRL B-3088<sup>T</sup> [SSU Clade 103] / WC21] Streptomyces lividans TK24 Streptomyces rameus NRRL B-16924<sup>T</sup> [SSU Clade 116] Streptomyces diastaticus subsp. ardesiacus NRRL B-1773<sup>1</sup>
 Streptomyces olivaceus NRRL B-3003<sup>1</sup>
 Streptomyces olivaceus NRRL B-1224<sup>1</sup>
 Streptomyces olivaceus NRRL B-1224<sup>1</sup> Streptomyces orivaceus NRRL B-1224' J
 Streptomyces enissocaesilis NRRL B-16365' [SSU Clade 41]
 Streptomyces geysifiensis NRRL B-12102' [SSU Clade 119]
 Streptomyces rochei NRRL B-2410' [SSU Clade 119 / WC12]
 Streptomyces mutabilis NRRL ISP-5470' [SSU Clade 119 / WC12]
 Streptomyces mutabilis NRRL ISP-5169' [SSU Clade 119 / WC12]
 Streptomyces nucleus NRRL B-1334'
 Streptomyces nucleus NRRL B-1334' Streptomyces rochei Streptomyces parvilus NRRL B-1628<sup>†</sup>
Streptomyces daghestanicus NRRL B-5418<sup>†</sup>
Streptomyces griseoviridis NRRL ISP-5229<sup>†</sup>
(SSU Clade 90 / WC17)
Streptomyces griseoviridis 

 Image: Streptomyces griseoviridis
 Streptomyces griseoviridis

 100
 Streptomyces griseoviridis

 101
 Streptomyces griseoviridis

 102
 Streptomyces curacia NRRL B-3280'

 Streptomyces curacia Streptomyces curacia Streptomyces sclerotialus

 101
 Streptomyces curacia Streptomyces sclerotialus Streptomyces sclerotialus Streptomyces sclerotialus Streptomyces sclerotialus Streptomyces sclerotialus NRRL B-2317]

 101
 Streptomyces sclerotialus NRRL B-2317]

 102
 Streptomyces sclerotialus NRRL B-2317]

 103
 Streptomyces sclerotialus NRRL B-2317]

 104
 Streptomyces sclerotialus NRRL B-2317]

 105
 Streptomyces scleroticus NRRL B-2317]

 106
 Streptomyces minutiscleroticus NRRL B-21173 [SSU Clade 87 / WC15]

 105
 Streptomyces minutiscleroticus NRRL B-12202' [SSU Clade 87 / WC15]

 103
 Streptomyces bluensis NRRL ISP-5564'

 104
 Streptomyces bluensis NRRL B-2423'

 Streptomyces bluensis NRRL ISP-3564 Streptomyces glaneratus NRRL B-24293' Streptomyces schlaensis NRRL B-24964' Streptomyces chiaeensis NRRL B-24964' Streptomyces glaucescens NRRL B-2404' [SSU Clade 2 / WC24] Streptomyces glaucescens NRRL B-24333 [SSU Clade 98] Streptomyces glabcsus CGMCC 4.0320 [SSU Clade 38] Streptomyces glabcsus CGMCC 4.0320 [SSU Clade 38] Streptomyces glabcsus CGMCC 4.0320 [SSU Clade 38] Streptomyces achromogenes subsp. rubradiris NRRL 3061<sup>T</sup> [SSU Clade 117] - Streptomyces nogalater NRRL ISP-5546<sup>T</sup>

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Streptomyces eurythermus NRRL ISP-5014 <sup>1</sup> [SSU Clade 115 / WC23]     Streptomyces advenduigriseus NRRL ISP-5648 <sup>7</sup> [SSU Clade 115 / WC24]     Streptomyces achromogenes NRRL B-2120T     Streptomyces corchorusi NRRL B-75628 <sup>7</sup> [SSU Clade 2 / WC20]     Streptomyces corchorusi NRRL B-72280 <sup>7</sup> [SSU Clade 2 / WC20]     Streptomyces corchorusi NRRL B-72280 <sup>7</sup> [SSU Clade 2 / WC20]     Streptomyces corchorusi NRRL B-72280 <sup>7</sup> [SSU Clade 2 / WC20]     Streptomyces regensis NRRL B-72280 <sup>7</sup> [SSU Clade 2 / WC20]     Streptomyces conversion Streptomyces conversion (Streptomyces conversion)     Streptomyces conversion (Streptomyces conversin)	lis	
The property of the prope	nticus	
Image: Streptomyces burgoensis DSM 41781'         Streptomyces and points's streptomyces and points's streptomyces and points's streptomyces costaricanus NRRL B-5429' [SSU Clade 12 / WC12]           Image: Streptomyces muinus NRRL B-2286' [SSU Clade 12 / WC17]         Streptomyces muinus NRRL B-2286' [SSU Clade 12 / WC17]           Image: Streptomyces muinus NRRL B-3230' [SSU Clade 12 / WC17]         Streptomyces muinus NRRL B-3230' [SSU Clade 97 / WC31]           Image: Streptomyces muinus NRRL B-3230' [SSU Clade 97 / WC31]         Streptomyces muinus NRRL B-3230' [SSU Clade 87]           Image: Streptomyces wellingtoniae NRRL B-1503'         Streptomyces muinus NRRL B-303' [SSU Clade 87]		
100       — Streptomyces anandii NRRL B-3590'         Image: Streptomyces againshii NRRL B-1816'       [Image: Streptomyces againshii NRRL B-16921'         100       Streptomyces spiralis NRRL B-16922'         101       Streptomyces nodosus NRRL B-2371'         102       Streptomyces nodosus NRRL B-2371'         103       Streptomyces nodosus ATCC 14899'         104       Streptomyces nodosus ATCC 14899'		
Comparing the second seco		
100       Streptomyces filipinensis NRRL ISP-5112 <sup>1</sup> [SSU Clade 10 / WC30]         100       Streptomyces durantiogriseus NRRL B-3309 <sup>1</sup> (SSU Clade 10 / WC30]         101       Streptomyces aurantiogriseus NRRL B-5416 <sup>1</sup> 102       Streptomyces brasiliensis NRRL B-3327 <sup>1</sup> 103       Streptomyces thermocoprophilus NRRL B-24314 <sup>1</sup> 104       Streptomyces thermocoprophilus NRRL B-24314 <sup>1</sup> 105       Streptomyces prasmbergiensis NRRL B-2221 <sup>1</sup> [SSU Clade 6 / WSMC]         106       Streptomyces prasmbergiensis NRRL B-2212 <sup>1</sup> [SSU Clade 6 / WC37]	nus	
[1] Streptomyces emeiensis NRRL B-24621 [SSU Clade 6] [100] Streptomyces prasinopilosus NRRL B-2711 [SSU Clade 6 / WC37] Streptomyces prasinopilosus NRRL B-59128 <sup>1</sup>		
Streptomyces hirsutus NRRL ISP-5095 <sup>°</sup> [SSU Clade 6 / WC37]     Streptomyces hirsutus NRRL B-2713 <sup>°</sup> [SSU Clade 6 / WC37]     Streptomyces chlorus KACC 20902 <sup>°</sup> Streptomyces chlorus		
Streptomyces chiorus NRRL B-29197     Streptomyces viridis NRRL B-59133'     Streptomyces india NRRL B-59131'     Streptomyces plana RRL B-59131'     Streptomyces ghanaensis NRRL B-12104'     Streptomyces disconsider (NRL B-12104'     Streptomyces ghanaensis NRRL B-12104'		
Streptomyces grainaerus NRC 14072     Streptomyces viridosporus NRRL ISP-5243 <sup>1</sup> Streptomyces grasinosporus NRRL B-12431 <sup>1</sup> Streptomyces graminearus NRRL B-16369 <sup>7</sup> [SSU Clade 12]		
Image: Streptomyces griseomycini NRRL B-5421 <sup>1</sup> [SSU Clade 104 / WC12]       Streptomyces griseostramineus NRRL B-5422 <sup>1</sup> [SSU Clade 104 / WC60]         Image: Streptomyces finbriatus NRRL B-3175 <sup>1</sup> Streptomyces griseostramineus NRRL B-3175 <sup>1</sup> Image: Streptomyces chryseus NRRL B-12347 <sup>1</sup> [SSU Clade 41 / WC17]       Streptomyces thermoviolaceus NRRL B-12374 <sup>1</sup>	ycini	
108 L Streptomyces thermodiastaticus NRRL B-5316' Streptomyces chirorobus NRRL B-24196' Streptomyces chirorobus NRRL 8144' Streptomyces thermoaitcaliloterans NRRL B-24315' [SSU Clade 105] Streptomyces thermoaitficians NRRL B-12534' [SSU Clade 105 / WC36] Streptomyces thermovulgaris NRRL B-12375' [SSU Clade 105 / WC36] Streptomyces thermovulgaris NRRL B-12375' [SSU Clade 105 / WC36] Streptomyces thermogriseus NRRL B-12372' [SSU Clade 105 / WC36] Streptomyces thermogriseus NRRL B-24322' [SSU Clade 105]	ermovulgaris	

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Streptomyces bullii NRRL B-24996' <u>100</u> Streptomyces cacaoi subsp. asoensis NRRL B-16592 <sup>T</sup> [SSU Clade 21]     Streptomyces lateritius NRRL B-5349 <sup>T</sup> [SSU Clade40 / WSMC]			
s hop Streptomyces iakyrus NRRL B-3317 <sup>7</sup> [SSU Clade 97] [] [] Streptomyces iakyrus NRRL ISP-5482 <sup>7</sup> [SSU Clade 97]] [] [] [] Utreptomyces paradoxus NRRL B-3457 <sup>7</sup>			
7			
1			
100         Streptomyces ciscaucasicus NRRL ISP-5275 [SSU Clade 8]         Streptomyces clavifer           Streptomyces canus NRRL B-3980 [SSU Clade 8 / WC25]         100         Streptomyces clavifer			

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<sup>99</sup> Streptomyces scabiei NRRL B-16523 <sup>T</sup> [SSU Clade 25 / WC3]			
L L Streptomyces europaeiscabiei NRRL B-24443 <sup>7</sup> [SSU Clade 25]			
Streptomyces ossamyceticus NRRL B-3822 <sup>†</sup> [SSU Clade 23]			
100 Streptomyces torulosus NRRL B-3889' [SSU Clade 23]			
100 Streptomyces acidiscabies NRRL B-16524' [SSU Clade 5]			
E Streptomycon griegoryther NBPL B 1919 <sup>T</sup> [SSU] Clode 4 / W(C21) ]			
<sup>3ª</sup> <sup>100</sup> Streptomyces griseoruber DSM 40281 <sup>™</sup>			
Streptomyces antibioticus DSM 40234'			
100 Streptomyces humidus NRRL B-3172 <sup>T</sup> [SSU Clade 21 / WC19]			
Streptomyces resistomycificus NRRL 2290 <sup>T</sup>			
Streptomyces resistomycificus DSM 40133 <sup>T</sup> Streptomyces resistomycificus			
Streptomyces resistomycificus NRRL ISP-5133 <sup>1</sup> Streptomyces jietaisiensis NRRL B-24616 <sup>7</sup> [SSU Clade 94]			
Streptomyces aurantiacus NRRL ISP-5412 <sup>7</sup> [SSU Clade 19 / WC45]			
Streptomyces tauricus NRRL B-12497 <sup>T</sup> [SSU Clade 19 / WC19]			
95 100 Streptomyces mirabilis NRRL B-2400 <sup>7</sup> [SSU Clade 20 / WC19]			
100 Streptomyces niveoruber NRRL B-2724 <sup>™</sup> [SSU Clade 9]			
Streptomyces phaeochromogenes NRRL B-1248 [SSU Clade 18 / WC41] [96] [100 Streptomyces phaeochromogenes NRRL B-3010' [SSU Clade 18 / WC41]] Streptomyces phaeochromogenes			
□ Streptomyces umbrinus NRRL B-2572 <sup>5</sup> [SSU Clade 18 / WC21]			
Streptomyces ederensis NRRL B-8146 <sup>1</sup> [SSU Clade 18]			
Streptomyces reticuliscabiei NRRL B-24446 <sup>1</sup> [SSU Clade 22]			
□ 100 Streptomyces graminilatus NRRL B-59124 <sup>™</sup>			
Streptomyces cinereus NRRL B-2909 <sup>1</sup> [SSU Clade 16 / WC19]			
Streptomyces flaveus NRRL B-16074 <sup>T</sup> [SSU Clade 16 / WC19] <u>100</u> [Streptomyces yerevanensis NRRL B-16943 <sup>T</sup> [SSU Clade 16 / WSMC]			
Streptomyces vastus NRRL B-12232 <sup>1</sup> [SSU Clade 16 / WC10]			
<sup>100</sup> Streptomyces pseudoechinosporeus NRRL B-16931 <sup>T</sup> [SSU Clade 84]			
100] Streptomyces virginiae CGMCC 4.1530 <sup>1</sup> [SSU Clade 39 / WC61] 100 <sup>1</sup> Streptomyces virginiae NRRL ISP-5094 <sup>1</sup> [SSU Clade 39 / WC61] <b>Streptomyces virginiae</b>			
Streptomyces flavotricini NRRL B-5419 <sup>T</sup> [SSU Clade 38 / WC61]			
d – Streptomyces noiiriensis CGMCC 4 1897 <sup>1</sup> ISSU Clade 391			
Streptomyces spororaveus CGMCC 4.1926 <sup>T</sup> [SSU Clade 39]     Streptomyces spororaveus NRRL B-16378 <sup>T</sup> [SSU Clade 39]     Streptomyces spororaveus			
Instreptomyces spororaveus NRRL B-15/38 [SSU Clade 39]     Streptomyces avidnii NRRL ISP-5526 <sup>5</sup> [SSU Clade 39]     Streptomyces substitus CGM/CC 4/184 <sup>5</sup> [SSU Clade 39]			
Image: Streptomyces xanthophaeus NRRL B-5414' [SSU Clade 39 / WC61] Streptomyces majorciensis' NRRL 15167			
Streptomyces goshikiensis NRRL B-5428 <sup>7</sup> [SSU Clade 39 / WC61]			
Streptomyces cirratus CGMCC 4.1679 <sup>T</sup> [SSU Clade 39 / WC62]			
100] Streptomyces katrae NRRL B-3093 <sup>1</sup> [SSU Clade 38 / WC61] 100] Streptomyces katrae NRRL ISP-5550 <sup>1</sup> [SSU Clade 38 / WC61] Streptomyces katrae			
I I I Streptomyces polychromogenes NRRL B-2656 ISSU Clade 387 WC611			
97 100 Streptomyces racemochromogenes NRRL B-5430 <sup>1</sup> [SSU Clade 38 / WC61]			
L Streptomyces colombiensis NRRL B-1990 <sup>7</sup> [SSU Clade 39 / WC61] Streptomyces lavendulae subsp. grasserius NRRL B-3072 <sup>7</sup> [SSU Clade 39]			
$\downarrow_{7}$ $\Box$ Streptomyces griseoflavus NRRL B-5312 <sup>T</sup>			
Streptomyces beijiangensis NRRL B-24307			
1000 Streptomyces mauvecolor CGMCC 4.1997 <sup>™</sup> [SSU Clade 29] 1001 Streptomyces mauvecolor NRRL B-24302 <sup>™</sup> [SSU Clade 29] ] <b>Streptomyces mauvecolor</b>			
100 └ Streptomyces violascens NRRL B-2700 <sup>™</sup> [SSU Clade 29]			
Streptomyces michiganensis NRRL B-1940 <sup>T</sup> [SSU Clade 29 / WC6]			
1001 Streptomyces xanthochromogenes NRRL B-5410 <sup>7</sup> [SSU Clade 29 / WC63] Streptomyces graminofaciens CGMCC 4.1359 <sup>7</sup> [SSU Clade 28 / WC26]			
Streptomyces peucetius CGMCC 4.1799 <sup>T</sup> [SSU Clade 28] Streptomyces peucetius			
Streptomyces peucetius NRRL B-3826' [SSU Clade 28]			
100L Streptomyces xantholiticus NRRL B-12153 <sup>T</sup> [SSU Clade 28 / WC24] Streptomyces amakusaensis NRRL B-3351 <sup>T</sup> [SSU Clade 47 / WSMC]			
Streptomyces clavuligerus NRRL 3585 <sup>T</sup>			
100 Streptomyces tsukubensis NRRL 18488			
Streptomyces crystallinus NRRL B-3629'     Imin Streptomyces melanogenes NRRL B-2072 <sup>T</sup> [SSU Clade 30 / WC33]     Streptomyces melanogenes			
Streptomyces noboritoensis NRRL B-12152 <sup>1</sup> (SSU Clade 30 / WC33]			
Streptomyces polyantibioticus NRRL B-24448 <sup>T</sup>			

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Streptomyces vinaceus CGMCC 4.1305 <sup>T</sup> [SSU Clade 39 / WC6] Streptomyces sioyaensis CGMCC 4.1306 <sup>T</sup> Streptomyces galilaeus CGMCC 4.1320 <sup>T</sup> [SSU Clade 13 / WC19] Streptomyces glisus J1074 Streptomyces glisus J1074 Streptomyces glisus J1074 Streptomyces lineus Subsp. solvifaciens NRRL B-1561 <sup>T</sup> [SSU Clade 112] Streptomyces lineus CGMCC 4.1677 <sup>T</sup> [SSU Clade 112] Streptomyces lineus NRRC 12790 <sup>T</sup> [SSU Clade 112] Streptomyces lineus NBRC 13083 <sup>T</sup> [SSU Clade 112] Streptomyces globisporus subsp. caucasicus NBRC 100770 <sup>T</sup> [SSU Clade 112] Streptomyces globisporus subsp. caucasicus NBRC 100770 <sup>T</sup> [SSU Clade 112] Streptomyces codorifer NBRC 13365 <sup>T</sup> [SSU Clade 112] Streptomyces codorifer NBRC 13365 <sup>T</sup> [SSU Clade 112] Streptomyces codorifer NBRL B-1328 <sup>T</sup> [SSU Clade 112] Streptomyces comescence CGMCC 4.1615 <sup>T</sup> [SSU Clade 112] Streptomyces champavati CGMCC 4.1615 <sup>T</sup> [SSU Clade 112] Streptomyces albus subsp. chroleucus' NRRL B-1813 <sup>T</sup> Streptomyces albus subsp. chroleucus' NRRL B-1813 <sup>T</sup> Streptomyces argentedus CGMCC 4.1693 <sup>T</sup> [SSU Clade 113 / WC18] Streptomyces argentedus CGMCC 4.1693 <sup>T</sup>	Streptomyces albidoflavus		
100 Streptomyces diastaticus NRRL B-1241 <sup>T</sup> [SSU Clade 113 / WC19]			
Streptomyces gougerotii NRRL B-1344 <sup>†</sup> [SSU Clade 113 / WC1B] Streptomyces rutgersensis NRRL B-2102 <sup>†</sup> [SSU Clade 113 / WC1B]			
100 Streptomyces pulveraceus CGMCC 4.1928 <sup>1</sup> [SSU Clade 35] 100 Streptomyces sanglieri NRRL B-24279 <sup>1</sup> [SSU Clade 35]			
Streptomyces atratus CGMCC 4.1632 <sup>1</sup> [SSU Clade 35]			
Streptomyces yanii CGMCC 4.1146 <sup>T</sup> [SSU Clade 35]			
Image: Streptomyces laculatispora NRRL B-24909'           Image: Streptomyces drozdowiczii NRRL B-24297'			
└ Streptomyces deserti NRRL B-24858'			
Streptomyces brevispora NRRL B-24910 <sup>1</sup> Streptomyces fulvorobeus JCM 9090 <sup>T</sup>			
Streptomyces atroolivaceus CGMCC 4.1405 <sup>T</sup> [SSU Clade 34 / WC3]			
Streptomyces olivoviridis CGMCC 4.0855	ptomyces atroolivaceus		
99 L Streptomyces mutomycini CGMCC 4.1747 <sup>™</sup> [SSU Clade 34]			
98 98 100 'Kitasatospora papulosa' NRRL B-16504 Streptomyces pratensis			
Streptomyces finlayi CGMCC 4.1436 <sup>T</sup> Streptomyces finlayi CGMCC 4.1436 <sup>T</sup>			
Streptomyces nitrosporeus CGMCC 4.0608 ] Streptomyces nitrosporeus			
Streptomyces nitrosporeus NRRL B-1316' Streptomyces mitosporeus Streptomyces griseolus CGMCC 4.1864 <sup>T</sup> [SSU Clade 36 / WC1C]			
100 Streptomyces halstedii NRRL B-1238 <sup>T</sup> [SSU Clade 36 / WC1C] Streptomyces	shalstedii		
Streptomyces halstedii NRRL ISP-5068 <sup>7</sup> [SSU Clade 36 / WC1C] Streptomyces griseolus NRRL B-2925 <sup>7</sup> [SSU Clade 36 / WC1C]			
Streptomyces flavogriseus CGMCC 4.1884 <sup>†</sup> [SSU Clade 37 / WC61] Streptomyces flavovirens CGMCC 4.0575 <sup>†</sup> [SSU Clade 37 / WC1C]			
Streptomyces nigrifaciens NRRL B-2094 <sup>T</sup> [SSU Clade 37 / WC1C]	vces flavovirens		
Streptomyces flavovirens NRRL B-1329 <sup>†</sup> [SSU Clade 37 / WC1C] J Streptomyces californicus CGMCC 4.0570 <sup>†</sup> [SSU Clade 33 / WC9]			
100 Streptomyces californicus NRRL B-2098 <sup>T</sup> [SSU Clade 33 / WC9]			
Streptomyces californicus NRRL B-2988 <sup>1</sup> [SSU Clade 33 / WC9] Streptomyces californicus NRRL B-1221 <sup>1</sup> [SSU Clade 33 / WC9]			
	tomyces puniceus		
100 Streptomyces puniceus NRRL B-2895 <sup>T</sup> [SSU Clade 33]			
Streptomyces floridae CGMCC 4.1972 <sup>1</sup> [SSU Clade 33 / WC9] Streptomyces floridae NRRL 2423 <sup>T</sup> [SSU Clade 33 / WC9]			
100 <sup>-</sup> Streptomyces sindenensis CGMCC 4.0626 <sup>T</sup>			
L Streptomyces badius CGMCC 4.1406'	2		
Streptomyces bacillaris CGMCC 4.1584 <sup><math>T</math></sup>			
UL 1907 Teptomyces bacillaris NRRL B-3038 <sup>1</sup> Streptomyces cavourensis subsp. cavourensis NRRL ISP-5300 <sup>1</sup> [SSU Clade 31 / WC1B]			
Streptomyces parvus CGMCC 4.0610			
Streptomyces albovinaceus CGMCC 4.1631 <sup>T</sup> Streptomyces albovinaceus NRRL ISP-5136 <sup>T</sup>			
Streptomyces globisporus subsp. globisporus NRRL B-2872 <sup>T</sup> Streptomyces griseinus CGMCC 4.1875 <sup>T</sup> Streptomyces a			
Streptomyces griseinus CGMCC 4.1875 Streptomyces a	libovinaceus		

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<ul> <li>96 ↓ <sup>100</sup> Streptomyces griseinus NRRL ISP-5047<sup>T</sup></li> <li>Streptomyces mediolani CGMCC 4.1896<sup>T</sup></li> <li>Streptomyces mediolani NRRL WC-3934<sup>T</sup></li> </ul>	Streptomyces albovinaceus	
Streptomyces fimicarius CGMCC 4.1629 <sup>T</sup> Streptomyces fimicarius NRRL ISP-5322 <sup>T</sup> Streptomyces caviscabies CGMCC 4.1836 <sup>T</sup> Streptomyces acrimycini CGMCC 4.1673 <sup>T</sup> Streptomyces bohaiensis NRRL B-24956 <sup>T</sup> Streptomyces baarnensis CGMCC 4.1607 <sup>T</sup> Streptomyces baarnensis NRRL B-1902 <sup>T</sup> Streptomyces flavofuscus CGMCC 4.1938 <sup>T</sup>	Streptomyces fimicarius	
Streptomyces ornatus CGMCC 4.1321 <sup>T</sup> <sup>110</sup> Streptomyces erumpens CGMCC 4.1626 <sup>T</sup> <sup>100</sup> Streptomyces setonii CGMCC 4.1367 <sup>T</sup> <sup>100</sup> Streptomyces setonii NRRL B-2555 <sup>T</sup>	Streptomyces griseus	
<ul> <li>Streptomyces setonii NRRL B-2555</li> <li>Streptomyces griseus subsp. griseus NRRL B-2682<sup>T</sup> Streptomyces griseus subsp. griseus CGMCC 4.1419<sup>T</sup> Streptomyces anulatus CGMCC 4.1421<sup>T</sup> Streptomyces anulatus CGMCC 4.1421<sup>T</sup> Streptomyces praecox CGMCC 4.1421<sup>T</sup> Streptomyces praecox NRRL B-2000<sup>T</sup> Streptomyces praecox NRRL B-1586<sup>T</sup> - Streptomyces chrysomallus subsp. chrysomallus NRRL 2250<sup>T</sup> Streptomyces chrysomallus subsp. chrysomallus NRRL 2250<sup>T</sup> Streptomyces chrysomallus subsp. chrysomallus ATCC 11523<sup>T</sup> Streptomyces chrysomallus subsp. chrysomallus ATCC 11523<sup>T</sup> Streptomyces chrysomallus Streptomyces chrysomallus Streptomyces chrysomallus ATCC 11523<sup>T</sup> Streptomyces chrysomallus CGMCC 4.1612<sup>T</sup> Streptomyces cyaneofuscatus CGMCC 4.1612<sup>T</sup> Streptomyces cavourensis subsp. washingtonensis CGMCC 4.1635<sup>T</sup> Streptomyces griseus subsp. alpha NRRL B-2249<sup>T</sup> Streptomyces griseus subsp. alpha NRRL B-2249<sup>T</sup> Streptomyces albus subsp. cretoceus NRRL B-1812<sup>T</sup> Streptomyces griseus subsp. cretosus NRRL B-2252<sup>T</sup> Streptomyces albus subsp. cretosus NRRL B-2252<sup>T</sup> Streptomyces albus subsp. cretosus NRRL B-2252<sup>T</sup> Streptomyces alboviridis CGMCC 4.1627<sup>T</sup> Streptomyces alboviridis NRRL B-1667<sup>T</sup> Streptomyces thioluteus NRRL B-1667<sup>T</sup></li> </ul>		
<ul> <li>Streptomyces abovinus NNNE B-3033</li> <li>Streptomyces fulvissimus DSM 40593<sup>T</sup> [SSU ( Streptomyces luridiscabiei LMG 21390<sup>T</sup></li> <li>Streptomyces luridiscabiei NRRL B-24455<sup>T</sup></li> </ul>	Clade 95 / WSMC]	

#### Fig. 1 a-j.

Phylogenetic relationships among strains within the *Streptomycetaceae* were constructed in IQ-Tree version 1.4.2 (Nguyen et al. 2015) using the Maximum Likelihood based on the full partition General Time Reversible model (Nei and Kumar 2000) including invariate sites plus a discrete Gamma model with 4 rate categories (GTR + F + I + G4) with separate branch lengths and models between partitions, which had been determined to be the optimal model considering the 5 gene partitions of these data during the model test phase of analysis. The trees were subjected to 1000 ultrafast bootstrap replications (Minh et al. 2013) and SH-like average likelihood ratio test replications (SH-aLRT) (Guindon et al. 2010). Bootstrap values less than 95% and/or SH-aLRT less than 85% were omitted as suggested by the IQ-Tree developers. Bar scale reflects number of substitutions per sites